19. **Crossing borders - how *Streptococcus suis* invades the brain**

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Streptococcus suis (*S. suis*) is a globally emerging zoonotic pathogen that can cause invasive disease commonly associated with meningitis in pigs and humans. To cause meningitis, *S. suis* must cross multiple host barriers - disrupting epithelial barriers, disseminating in the bloodstream, and crossing the specialised microvasculature of the central nervous system known as the blood brain barrier (BBB). Another proposed entry point to the brain is the choroid plexus epithelium. Previous studies have shown that surface enolase of *S. suis* can bind to serum plasminogen which can be converted to plasmin a host protease that degrades extracellular matrix proteins. We hypothesize that *S. suis* exploits plasminogen to degrade the basement membrane matrix of the brain microvasculature and choroid plexus to invade the brain and cause meningitis. To this end, we identified possible plasminogen-binding sites of *S. suis* enolase by *in silico* prediction and experimental validation. We exploited the microvascular endothelium hCMEC/D3 cell line as the *in vitro* BBB model to study the role of enolase-plasminogen interaction in *S. suis* invasion. All ENO^{mut} *S. suis* mutant strains we constructed were observed to significantly reduce the plasminogen binding and plasmin binding. We selected two mutants with the most impaired plasminogen-binding ability for *in vitro* tests. In the hCMEC/D3 cell monolayer, the bacterial translocation was facilitated when active plasmin was bound on the surface of wild-type *S. suis*, while no significant improvement of translocation was observed in both ENO^{mut} *S. suis* mutants. Taken together, these results highlight the function of enolase in *S. suis* invades the brain. We will also describe the development of induced pluripotent stem cell (iPSC)-derived endothelium and choroid plexus organoids as *in vitro* models to further explore the virulence mechanisms by which *S. suis* causes meningitis.